

of a first Office Action on the merits of the above-identified application, or before the mailing date of a first Office Action after the filing of request for continued examination under § 1.114, no additional fee is required.

☐ In accordance with § 1.129(a), this Information Disclosure Statement is being filed in connection with ☐ the first or ☐ second After Final Submission, therefore:

☐ Certification in Accordance with § 1.97(e) is attached; or

☐ The fee of \$180.00 as set forth in § 1.17(p) is attached.

☐ In accordance with § 1.97(c), this Information Disclosure Statement is being filed after the period set forth in § 1.97(b) above but before the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311, or before an action that otherwise closes prosecution in the application, therefore:

☐ Certification in Accordance with § 1.97(e) is attached;
or

☐ The fee of \$180.00 as set forth in § 1.17(p) is attached.

☐ In accordance with § 1.97(d), this Information Disclosure Statement is being filed after the mailing date of either a Final Action under § 1.113 or a Notice of Allowance under § 1.311 but before, or simultaneously with, the payment of the Issue Fee, therefore included are: Certification in Accordance with § 1.97(e); and the submission fee of \$180.00 as set forth in § 1.17(p).

☐ Copies of each of the references listed on the attached Form PTO-1449 are enclosed herewith.

☒ Copies of references listed on the attached Form PTO-1449 are enclosed herewith

EXCEPT THAT:

☒ In view of the voluminous nature of references 104-105, and the likelihood that these references are available to the Examiner, copies are not enclosed herewith.

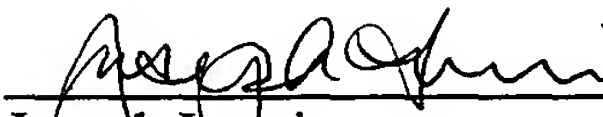
☒ In accordance with § 1.98(d), copies of the following references listed on the attached Form PTO-1449 are not enclosed herewith because they were previously cited by or submitted to the U.S. Patent and Trademark Office in patent application(s) for which a claim for priority under 35 U.S.C. § 120 have been made in the instant application:

☒ Copies of references 1-169 listed on the attached Form PTO-1449 were previously cited by or submitted to the Patent and Trademark Office in prior Application No. 09/409,926, filed **September 30, 1999.**

Please charge any deficiency or credit any overpayment to Deposit Account No. 23-3050. This form is submitted in duplicate.

- ☐ The relevance of those listed references which are not in the English language is as follows:
- ☒ There are no listed references which are not in the English language.

Date: AUG. 14, 2003



Joseph Lucci
Registration No. 33,307

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	1	Abe, A. et al., "Conformational Energies and the Random-Coil Dimensions and Dipole Moments of Polyoxides $\text{CH}_3\text{O}[(\text{CH}_2)]_x\text{OCH}_3$," <i>J. Am. Chem. Soc.</i> , 1976 , 6468-6476	
	2	Agrawal, Sudhir, et al., "Site-specific excision from RNA by Rnase H and mixed-phosphate-backbone oligodeoxynucleotides," <i>Proc. Nutl. Acad. Sci. USA</i> , 1990 , 87, 1401-1405	
	3	Baker, B.F. et al., "2'-O-(2-Methoxy)ethyl-modified Anti-intercellular Adhesion Molecule 1 (ICAM-1) Oligonucleotides Selectively Increase the ICAM-1 Translation Initiation Complex in Human Umbilical Vein Endothelial Cells", <i>J. Biol. Chem.</i> , 1997 , 272, 11994-12000	
	4	Berger, I. et al., "Crystal structures of B-DNA with incorporated 2'-deoxy-2'-fluoro-arabino-furanosyl thymines: implications of conformational preorganization for duplex stability," <i>Nucl. Acids Res.</i> , 1998 , 26(10), 2473-2480	
	5	Blake et al., "Hybridization Arrest of Globin Synthesis in Rabbit Reticulocyte Lysates and Cells by Oligodeoxyribonucleoside Methylphosphonates," <i>Biochem.</i> , 1985 , 24, 6139-4145	
	6	Busen, W., The Subunit Structure of Calf Thymus Ribonuclease HI As Revealed by Immunological Analysis," <i>J. Biol. Chem.</i> , 1982 , 257(12), 7106-7108	
	7	Busen, W. et al., "Distinct Ribonuclease H Activities in Claf Thymus," <i>Eur. J. Biochem.</i> , 1975 , 52, 179-190	
	8	Busen, W., "Purification, Subunit Structure, and Serological Analysis of Calf Thymus Ribonuclease HI," <i>J. Biol. Chem.</i> , 1980 , 255(19), 9434-9443	
	9	Busen et al., "Ribonuclease H Levels during the Response of Bovine Lymphocytes to Concanavalin A," <i>Eur. J. Biochem.</i> , 1977 , 74, 203-208	
	10	Cazenave et al., "Comparative inhibition of rabbit globin mRNA translation by modified antisense oligodeoxynucleotides," <i>Nucleic Acid Res.</i> , 1989 , 17(11), 4255-4273	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	11	Cook, P.D., "Medicinal Chemistry of Antisense Oligonucleotides - future opportunities", <i>Anti-Cancer Drug Design</i> , 1991 , 6, 585-607	
	12	Cornell, W. D. et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules," <i>J. Am. Chem. Soc.</i> , 1995 , 117, 5179-5197	
	13	Cory, A.H. et al., "2'-Deoxy-2'-Methylene Derivatives of Adenosine, Guanosine, Tubercidin, Cytidine and Uridine as Inhibitors of L1210 Cell Growth in Culture," <i>Biochemical Pharmacology</i> , 1994 , 47(2), 365-371	
	14	Cowser, L. M. et al., "In vitro and In Vivo Activity of Antisense Inhibitors of ras: Potential for Clinical Development," <i>Anti-Cancer Drug Design</i> , 1997 , 12, 359-371	
	15	Crooke, S.T. et al., "Kinetic characteristics of <i>Escherichia coli</i> RNase H1: cleavage of various antisense oligonucleotide-RNA duplexes", <i>Biochem. J.</i> , 1995 , 312, 599-608	
	16	Crooke, S.T. et al., "Pharmacokinetic Properties of Several Novel Oligonucleotide Analogs in mice", <i>J. Pharmacol. Exp. Therapeutics</i> , 1996 , 277, 923-937	
	17	Crouch, R. J. et al., <i>Nuclease</i> , Linn, S.M. et al. (eds.), Cold Spring Harbor Laboratory Press, Plainview, NY, 1982 , 211-241	
	18	Damha, M.J. et al., "An improved procedure for derivatization of controlled-pore glass beads for solid-phase oligonucleotide synthesis", <i>Nucl. Acids Res.</i> , 1990 , 18, 3813-3821	
	19	Damha, M.J. et al., "Hybrids of RNA and Arabinonucleic Acids (ANA and 2'F-ANA) Are Substrates of Ribonuclease H," <i>J. Am. Chem. Soc.</i> , 1998 , 120, 12976-12977	
	20	Dash et al., "Selective elimination of mRNAs <i>in vivo</i> : Complementary oligodeoxynucleotides promote RNA degradation by an RNase H-like activity," <i>Proc. Nat'l Acad. Sci. USA</i> , 1987 , 84, 7896-7900	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	21	De Mesmaeker, A. et al., "Antisense Oligonucleotides", <i>Acc. Chem. Res.</i> , 1995 , 28, 366-374	
	22	Dean, N.M. et al., "Inhibition of protein kinase C- α expression in mice after systemic administration of phosphorothioate antisense oligodeoxynucleotides", <i>Proc. Natl. Acad. Sci.</i> , 1994 , 91, 11762-11766	
	23	Delgado, C. et al., "The Uses and Properties of PEG-Linked Proteins", <i>Crit. Rev. in Therapeutic Drug Carrier Sys.</i> , 1992 , 9, 249-304	
	24	Dimock, S. et al., "An Efficient Multigram Synthesis of Monomers for the Preparation of Novel Oligonucleotides Containing Isosteric Non-Phosphorous Backbones," <i>Nucleosides & Nucleotides</i> , 1997 , 16(7-9), 1629-1632	
	25	Eder et al., "Substrate specificity of human RNase H1 and its role in excision repair of ribose residues misincorporated in DNA," <i>Biochimie</i> , 1993 , 75, 123-126	
	26	Flanagan, W.M. et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," <i>Nature Biotechnology</i> , 1999 , 17, 48-52	
	27	Frank et al., "Purification and characterization of human ribonuclease HII," <i>Nucleic Acids Res.</i> , 1994 , 22(24), 5247-5254	
	28	Fraser, A. et al., "Synthesis and Conformational Properties of 2'-Deoxy-2'-methylthiopyrimidine and-purine Nucleosides: Potential Antisense Applications," <i>J. Heterocyclic Chem.</i> , 1993 , 30, 1277-1287	
	29	Freier, S.M. et al., "The ups and downs of nucleic acid duplex stability: structure-stability studies on chemically-modified DNA:RNA duplexes", <i>Nucl. Acids Res.</i> , 1997 , 25, 4429-4443	
	30	Gaffney, B.L. et al., "A New Strategy for the Protection of Deoxyguanosine During Oligonucleotide Synthesis", <i>Tetrahedron Letts.</i> , 1982 , 23, 2257-2260	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	31	Gagnor, C. et. al., "α-DNA VI: Comparative Study of α- and β-Anomeric Oligodeoxyribonucleotides in Hybridization to mRNA and in Cell Free Translation Inhibition", <i>Nucl. Acids Res.</i> , 1987 , <i>15</i> , 10419-10436	
	32	Gotfredsen, C.H. et al., "Novel Oligodeoxynucleotide Analogues Containing A 2'-O-Methylarabinonucleoside," <i>Tetrahedron Letts.</i> , 1994 , <i>35</i> (37), 6941-6944	
	33	Gotfredsen, C.H. et al., "Synthesis and Properties of α- and β-Oligodeoxynucleotides Containing α- and β-1-(2-O-Methyl-D-arabino-furanosyl) thymine," <i>Bioorganic & Medicinal Chemistry</i> , 1996 , <i>4</i> (8), 1217-1225	
	34	Guzaev A. et al., "Synthesis of C-Radiolabeled Oligonucleotides with a Novel Phosphoramidite Reagent," <i>Bioorg. & Med. Chem. Lett.</i> , 1998 , <i>8</i> , 1123-1126	
	35	Hall, K. B. et al., "Thermodynamic and Structural Properties of Pentamer DNA·DNA, RNA·RNA, and DNA·RNA Duplexes of Identical Sequence," <i>Biochemistry</i> , 1991 , <i>30</i> , 10606-10613	
	36	Hamm, M. L. et al., "Incorporation of 2'-Deoxy-2'-mercaptocytidine into Oligonucleotides via Phosphoramidite Chemistry," <i>J. Org. Chem.</i> , 1997 , <i>62</i> , 3415-3420	
	37	Hansske, F. et al., "Nucleic Acid Related Compounds. 43. A Convenient Procedure for the Synthesis of 2' and 3'-Ketonucleosides," <i>Tetrahedron Letts.</i> , 1983 , <i>24</i> (15), 1589-1592	
	38	Hansske, F. et al., "2' and 3'-Ketonucleosides and their Arabino and Xylo Reduction Products", <i>Tetrahedron</i> , 1984 , <i>40</i> , 125-135	
	39	Hausen, P. et al., "Ribonuclease H: An Enzyme Degrading the RNA Moiety of DNA·RNA Hybrids," <i>Eur. J. Biochem.</i> , 1970 , <i>14</i> , 278-283	
	40	Iribarren, A.M. et al., "Resistance to Degradation by Nucleases of (2'S)-2'-Deoxy-2'-C-methyloligonucleotides, Novel Potential Antisense Probes," <i>Antisense Res. and Develop.</i> , 1994 , <i>4</i> , 95-98	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	41	Itaya, M., "Isolation and characterization of a second RNase H (RNase HII) of <i>Escherichia coli</i> K-12 encoded by the <i>rnhB</i> gene," <i>Proc. Natl. Acad. Sci. USA</i> , 1990, 87, 8587-8591	
	42	Itaya et al., "Selective cloning of genes encoding RNase H from <i>Salmonella typhimurium</i> , <i>Saccharomyces cerevisiae</i> and <i>Escherichia coli rnh</i> mutant," <i>Mol. Gen. Genet.</i> , 1991, 227, 438-445	
	43	Itaya, M. et al., "Molecular cloning of a ribonuclease H (RNase HI) gene from an extreme thermophile <i>Thermus thermophilus</i> HB8: a thermostable RNase H can functionally replace the <i>Escherichia coli</i> enzyme <i>in vivo</i> ," <i>Nucleic Acids Res.</i> , 1991, 19(16), 4443-4449	
	44	Iyer, R.P. et al., "The Automated Synthesis of Sulfur-Containing Oligodeoxyribonucleotides Using 3H-1,2-Benzodithiol-3-one 1,1-Dioxide as a Sulfur-Transfer Reagent", <i>J. Org. Chem.</i> , 1990, 55, 4693-4699	
	45	Kabanov, A.V., "A new class of antivirals: antisense oligonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", <i>FEBS Letts.</i> , 1990, 259, 327-330	
	46	Kanaya, S. et al., "Expression, Purification, and Characterization of a Recombinant Ribonuclease H from <i>Thermus thermophilus</i> HB8," <i>J. Biol. Chem.</i> , 1992, 267(14), 10184-10192	
	47	Kanaya et al., "Importance of the Positive Charge Cluster in <i>Escherichia coli</i> Ribonuclease HI for the Effective Binding of the Substrate," <i>J. Biol. Chem.</i> , 1991, 266(18), 11621-11627	
	48	Kane, C.M., "Renaturase and Ribonuclease H: A Novel Mechanism That Influences Transcript Displacement by RNA Polymerase II in Vitro," <i>Biochemistry</i> , 1988, 27, 3187-3196	
	49	Katayanagi et al., "Three-dimensional structure of ribonuclease H from <i>E. coli</i> ," <i>Nature</i> , 1990, 347, 306-309	
	50	Katayanagi et al., "Crystal Structure of <i>Escherichia coli</i> RNase HI in Complex With Mg^{2+} at 2.8 Å Resolution: Proof for a Single Mg^{2+} Binding Site," <i>Proteins: Struct., Funct., Genet.</i> , 1993, 17, 337-346	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	51	Kois, P. et al., "Synthesis and Some Properties of Modified Oligonucleotides. 2. Oligonucleotides Containing 2'-Deoxy-2'-Fluoro-B-D-Arabinofuranosyl Pyrimidine Nucleosides," <i>Nucleosides & Nucleotides</i> , 1993 , 12(10), 1093-1109	
	52	Kozak, M., "The Scanning Model for Translation: An Update," <i>J. Cell Biol.</i> , 1989 , 108, 229-241	
	53	Lane, A. N. et al., "NMR Assignments and Solution Conformation of the DNA-RNA Hybrid Duplex d(GTGAACCTT)-r(AAGUUCAC)," <i>Eur. J. Biochem.</i> , 1993 , 215, 297-306	
	54	Lesnik, E.A. et al., "Oligodeoxynucleotides Containing 2'-O-Modified Adenosine" Synthesis and Effects on Stability of DNA:RNA Duplexes", <i>Biochem.</i> , 1993 , 32, 7832-7838	
	55	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture", <i>Proc. Natl. Acad. Sci.</i> , 1989 , 86, 6553-6556	
	56	Lima, W.F. et al., "Binding Affinity and Specificity of Escherichia coli RNase H1: Impact on the Kinetics of Catalysis of Antisense Oligonucleotide-RNA Hybrids," <i>Biochemistry</i> , 1997 , 36, 390-398	
	57	Lima, W.F. et al., "The influence of Antisense Oligonucleotide-induced RNA Structure on <i>Escherichia coli</i> RNase H1 Activity," <i>J. Biol. Chem.</i> , 1997 , 272(29), 18191-18199	
	58	Lin, K.Y. et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," <i>J. Am. Chem. Soc.</i> , 1998 , 120, 8531-8532	
	59	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", <i>Annals NY Acad. Sciences</i> , 1992 , 660, 306-309	
	60	Manoharan, M. et al., "Lipidic Nucleic Acids", <i>Tetrahedron Letts.</i> , 1995 , 36, 3651-3654	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	61	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", <i>Nucleosides and Nucleotides</i> , 1995 , 14, 969-973	
	62	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications", <i>Bioorg. Med. Chem. Letts.</i> , 1993 , 3, 2765-2770	
	63	Manoharan M. et al., "Cholic Acid-Oligonucleotide Conjugates for Antisense Applications", <i>Bioorganic Med. Chem. Letts.</i> , 1994 , 4, 1053-1060	
	64	Martin, P., "Ein neuer Zugang zu 2'-O-Alkylribonucleosiden und Eigenschaften deren Oligonucleotide", <i>Helvetica Chemica Acta</i> , 1995 , 78, 486-504 (English abstract included)	
	65	Matsuda, A. et al., "Nucleosides and Nucleotides. 97. Synthesis of New Brand Spectrum Antineoplastic Nucleosides, 2'-Deoxy-2'-methylidenecytidine (DMDC) and Its Derivatives," <i>J. Med. Chem.</i> , 1991 , 34, 812-819	
	66	Mishra, R.K. et al., "Improved leishmanicidal effect of phosphorothioate antisense oligonucleotides by LDL-medicated delivery", <i>Biochim. Et Biophysica</i> , 1995 , 1264, 229-237	
	67	Monia, B.P. et al., "Evaluation of 2'-Modified Oligonucleotides Containing 2'-Deoxy Gaps as Antisense Inhibitors of Gene Expression", <i>J. Biol. Chem.</i> , 1993 , 268, 14514-14522	
	68	Monia, B.P. et al., "Sequence-specific Antitumor Activity of a Phosphorothioate Oligodeoxyribonucleotide Targeted to Human C-raf Kinase Supports an Antisense Mechanism of Action In Vivo," <i>Proc. Natl. Acad. Sci. USA</i> , 1996 , 93, 15481-15483	
	69	Nakamura et al., "How does Rnase H recognize a DNA-RNA hybrid?" <i>Proc. Natl. Acad. Sci. USA</i> , 1991 , 88, 11535-11539	
	70	Oberhauser, B. et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", <i>Nucl. Acids Res.</i> , 1992 , 20, 533-538	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	71	Obika, S. et al., "Preparation and Properties of 2',5'-Linked Oligonucleotide Analogues Containing 3'-O,4'-C-Methylenetriphosphonates," <i>Bioorg. Med. Chem. Letts.</i> , 1999 , 9, 515-518	
	72	Ouchi, T. et al., "Synthesis and Antitumor Activity of Poly(Ethylene Glycol)s Linked to 5'-Fluorouracil via a Urethane or Urea Bond", <i>Drug Des. & Disc.</i> , 1992 , 9, 93-105	
	73	Pardi et al., "Comparative Study of Ribonucleotide, Deoxyribonucleotide, and Hybrid Oligonucleotide Helices by Nuclear Magnetic Resonance," <i>Biochemistry</i> , 1981 , 20, 3986-3996	
	74	Polushin, N. N. et al., "Synthesis of Oligonucleotides Containing 2'-Azido- and 2'-Amino-2'-deoxyuridine Using Phosphotriester Chemistry," <i>Tetrahedron Letts.</i> , 1996 , 37(19), 3227-3230	
	75	Pon, R.T., "Solid Phase Supports for Oligonucleotide Synthesis", <i>Methods in Molecular Biology, Vol. 20, Protocols for Oligonucleotides and Analogs</i> , Agrawal, S. (ed.), Humana Press, Totowa, NJ, 1993 , Chapter 19, 465-496	
	76	Ravasio, N. et al., "Selective Hydrogenations Promoted by Copper Catalysts. 1. Chemoselectivity, Regioselectivity, and Stereoselectivity in the Hydrogenation of 3-Substituted Steroids", <i>J. Org. Chem.</i> , 1991 , 56, 4329-4333	
	77	Resmini, M. et al., "38. Nucleosides: Efficient Synthesis of Arabinoguanosine Building Blocks," <i>Helvetica Chimica Acta</i> , 1994 , 77, 429-434	
	78	Resmini, M. et al., "9. Nucleotides: Synthesis of Arabinonucleoside Phosphoramidite Building Blocks," <i>Helvetica Chimica Acta</i> , 1993 , 76, 158-167	
	79	Resmini, M. et al., "Synthesis of an Arabinonucleic Acid (tANA)," <i>Bioorgan. & Med. Chem. Letts.</i> , 1994 , 4(16), 1909-1912	
	80	Roberts, D. D. et al., "Neighboring-Group Study in Solvolyses of Cyclopentyl and Cyclohexyl Tosylates," <i>J. Org. Chem.</i> , 1969 , 34(8), 2415-2417	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office	Docket No. ISIS-5138	Application No. 10/616,009
	Applicant Stanley T. Crooke, et al.	
	Filing Date July 8, 2003	Group Not Yet Assigned
	Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)		
	81	Roberts, D. D. et al., "Neighboring Methoxy Group Effect in Solvolysis Reactions of Cyclopentyl and Cyclohexyl p-Toluenesulfonates," <i>J. Org. Chem.</i> , 1997 , 62, 1857-1859
	82	Robins, M.J. et al., "Nucleic Acid Related Compounds. 42. A General Procedure for the Efficient Deoxygenation of Secondary Alcohols. Regiospecific and Stereoselective Conversion of Ribonucleosides to 2'-Deoxynucleosides", <i>J. Am. Chem. Soc.</i> , 1983 , 105, 4059-4065
	83	Rong, Y. W. et al., "On the Molecular Weight and Subunit Composition of Calf Thymus Ribonuclease H1," <i>Biochemistry</i> , 1990 , 29, 383-389
	84	Rosenthal, A. et al., "Nucleosides of Branched-Chain Nitromethyl, Cyanomethyl, and Aminomethyl Sugars," <i>Tetrahedron Letts.</i> , 1970 , 48, 4233-4235
	85	Saison-Behmoaras, T. et al., "Short modified antisense oligonucleotides directed against Ha-ras point mutation induce selective cleavage of the mRNA and inhibit T24 cells proliferation", <i>EMBO J.</i> , 1991 , 10, 1111-1118
	86	Sanghvi, Y.S. et al., "Concept, Discovery and Development of MMI Linkage: Story of a Novel Linkage for Antisense Constructs," <i>Nucleosides & Nucleotides</i> , 1997 , 16(7-9), 907-916
	87	Schmit, C. et al., "The Effects of 2'-and 3'-Alkyl Substituents on Oligonucleotide Hybridization and Stability," <i>Bioorgan. & Med. Chem. Letts.</i> , 1994 , 4(16), 1969-1974
	88	Seela, F. et al., "Palindromic Octa-and Dodecanucleotides Containing 2'-Deoxytubercidin: Synthesis, Hairpin Formation, and Recognition by the Endodeoxyribonuclease <i>EcoRI</i> ", <i>Biochemistry</i> , 1987 , 26, 2232-2238
	89	Shea, R.G. et al., "Synthesis, hybridization properties and antiviral activity of lipid-oligodeoxynucleotide conjugates", <i>Nucl. Acids Res.</i> , 1990 , 18, 3777-3783
	90	Stein, H. et al., "Enzyme from Calf Thymus Degrading the RNA Moiety of DNA-RNA Hybrids: Effect on DNA-Dependent RNA Polymerase," <i>Science</i> , 1969 , 166, 393-395
EXAMINER		DATE CONSIDERED



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	91	Suck, D. et al., "Structure of DNase I at 2.0 Å resolution suggests a mechanism for binding to and cutting DNA," <i>Nature</i> , 1986, 321, 620-625	
	92	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups", <i>Biochimie</i> , 1993, 79, 49-54	
	93	Swayze, E. E. et al., "The Synthesis of N,N'-O-Trisubstituted Hydroxylamines via a Mild Reductive Alkylation Procedure: An Improved Synthesis of the MMI Backbone," <i>Synlett</i> , 1997, 859-861	
	94	Swayze, E. E. et al., "The Synthesis of the Sixteen Possible 2'-O-Methyl MMI Dimer Phosphoramidites: Building Blocks for the Synthesis of Novel Antisense Oligonucleotides," <i>Nucleosides & Nucleotides</i> , 1997, 16(7-9), 971-972	
	95	Thomson, J. B. et al., "Synthesis and Properties of Diuridine Phosphate Analogues Containing Thio and Amino Modifications," <i>J. Org. Chem.</i> , 1996, 61, 6273-6281	
	96	Tidd, D.M. et al., "Evaluation of N-ras oncogene antisense, sense, and nonsense sequence methylphosphonate oligonucleotide analogues", <i>Anti-Cancer Drug Design</i> , 1988, 3, 117-127	
	97	Tidd, D.M. et al., "Partial protection of oncogene, anti-sense oligodeoxynucleotides against serum nuclease degradation using terminal methylphosphonate groups", <i>Br. J. Cancer</i> , 1989, 60, 343-350	
	98	Wagner, D. et al., "Preparation and Synthesis Utility of Some Organotin Derivatives of Nucleosides", <i>J. Org. Chem.</i> , 1974, 39, 24-30	
	99	Walder, R. et al., "Role of RNase H in hybrid-arrested translation by antisense oligonucleotides", <i>Proc. Natl. Acad. Sci.</i> , 1988, 85, 5011-5015	
	100	Wintersberger, "Ribonucleases H of Retroviral and Cellular Origin," <i>Pharmac. Ther.</i> , 1990, 48, 259-280	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	101	Wolfe, S., "The Gauche Effect. Some Stereochemical Consequences of Adjacent Electron Pairs and Polar Bonds," <i>Accounts of Chemical Research</i> , 1972, 5, 102-110	
	102	Yang et al., "Structure of Ribonuclease H Phased at 2 Å Resolution by MAD Analysis of the Selenomethionyl Protein," <i>Science</i> , 1990, 249, 1398-1405	
*	103	Ausubel et al., <i>Current Protocols in Molecular Biology</i> , Wiley and Sons, New York, NY., 1988 and 1989	
*	104	Deutscher, M. P., <i>Guide to Protein Purification, Methods in Enzymology</i> , Academic Press, New York, NY, 182, 1990	
*	105	Sambrook, J. et al., <i>Molecular Cloning: A Laboratory Manual</i> , Cold Spring Harbor Laboratory Press, Plainview, 1989	
	106	Boado, R.J., et al., "Complete inactivation of target mRNA by biotinylated antisense oligodeoxynucleotide - avidin conjugates," <i>Bioconjugate Chem.</i> , 1994, 5, 406-410	
	107	Bordier, B., et al., "Sequence-specific inhibition of human immunodeficiency virus (HIV) reverse transcription by antisense oligonucleotides: comparative study in cell-free assays and in HIV-infected cells," <i>Proc. Natl. Acad. Sci. USA</i> , 1995, 92, 9383-9387	
	108	Chiang, M., et al., "Antisense oligonucleotides inhibit intercellular adhesion molecule 1 expression by two distinct mechanisms," <i>J. Biological Chemistry</i> , 1991, 266(27), 18162-18171	
	109	Dagle, J., et al., "Targeted degradation of mRNA in Xenopus oocytes and embryos directed by modified oligonucleotides: studies of An2 and cyclin in embryogenesis," <i>Nucleic Acids Res.</i> , 1990, 18(16), 4751-4757	
	110	Frank, P., et al., "Cloning, subcellular localization and functional expression of human Rnase HII, <i>Biol. Chem.</i> , 1998, 379, 1407-1412	
EXAMINER		DATE CONSIDERED	

*A copy of these references will not be forwarded to the U.S. Patent and Trademark Office since they are believed to be too voluminous and easily obtainable by the Examiner.



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	111	Frank, P., et al., "Cloning of the cDNA encoding the large subunit of human Rnase HI, a homologue of the prokaryotic Rnase HII," <i>Proc. Natl. Acad. Sci. USA</i> , 1998 , 95, 12872-12877	
	112	Furdon, P.J. et al., "Rnase H cleavage of RNA hybridized to oligonucleotides containing methylphosphonate, phosphorothioate and phosphodiester bonds," <i>Nucleic Acids Res.</i> , 1989 , 17, 9193-9204	
	113	Giles, R.V., "Increased specificity for antisense oligodeoxynucleotide targeting of RNA cleavage by Rnase H using chimeric methylphosphonodiester/phosphodiester structures," <i>Nucleic Acids Res.</i> , 1992 , 20(4), 763-770	
	114	Giles, R.V., "Enhanced Rnase H activity with methylphosphonodiester/phosphodiester chimeric antisense oligodeoxynucleotides," <i>Anti-Cancer Drug Design</i> , 1992 , 7, 37-48	
	115	Ghosh, M.K., et al., "Phosphorothioate-phosphodiester oligonucleotide co-polymers: assessment for antisense application," <i>Anti-Cancer Drug Design</i> , 1993 , 8, 15-32	
	116	Godard, G., et al., "Antisense effects of cholesterol-oligodeoxynucleotide conjugates associated with poly (alkylcyanoacrylate) nanoparticles," <i>Eur. J. Biochem.</i> , 1995 , 232, 404-410	
	117	Gottikh, M., et al, "αβ Chimeric antisense oligonucleotides: synthesis and nuclease resistance in biological media," <i>Antis. Res. And Dev.</i> , 1994 , 4, 251-258	
	118	Hoke, G.D., et al., "effects of phosphorothioate capping on antisense oligonucleotide stability, hybridization and antiviral efficacy versus herpes simplex virus infection," <i>Nucleic Acids Res.</i> , 1991 , 19(20), 5743-5748	
	119	Kawasaki, E.S., "Quantitative hybridization-arrest of mRNA in <i>Xenopus</i> oocytes using single-stranded complementary DNA or oligonucleotide probes," <i>Nucleic Acids Res.</i> , 1985 , 13(13), 4991-5005	
	120	Krainer, A.R., et al., "Multiple factors including the small nuclear ribonucleoproteins U1 and U2 are necessary for pre-mRNA splicing in vitro," <i>Cell</i> , 1985 , 42, 725-736	
EXAMINER		DATE CONSIDERED	



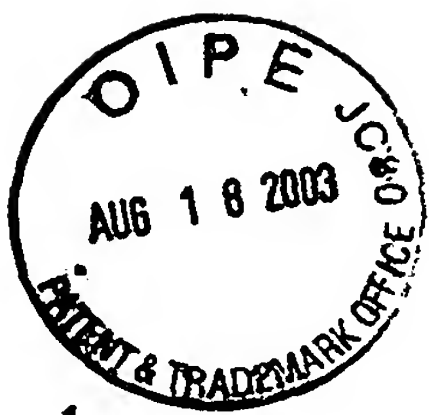
Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office		Docket No. ISIS-5138	Application No. 10/616,009
		Applicant Stanley T. Crooke, et al.	
		Filing Date July 8, 2003	Group Not Yet Assigned
		Confirmation No. Not Yet Assigned	
OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)			
	121	Lee, et al., "Antisense gene suppression against human ICAM-1, ELAM-1, and VCAM-1 in cultured human umbilical vein endothelial cells," <i>SHOCK</i> , 1995, 4(1), 1-10	
	122	Liu, P.K., et al., "Suppression of ischemia-induced fos expression and AP-1 activity by an antisense oligodeoxynucleotide to c-fos mRNA," <i>Am. Neurol. Assoc.</i> , 1994, 566-576	
	123	Quartin, R.S., et al., "Number and distribution of methylphosphonate linkages in oligodeoxynucleotides affect exo-and endonuclease sensitivity and ability to form RNase H substrates," <i>Nucleic Acids Res.</i> , 1989, 17(8), 7253-7262	
	124	Rosolen, A., et al., "Effect of over-expression of bacterial ribonuclease H on the utility of antisense MYC oligodeoxynucleotides in the monocytic leukemia cell line U937," <i>Biochimie</i> , 1993, 75, 79-87	
	125	Wu, H., et al., "Molecular cloning and expression of cDNA for human RNase H," <i>Antisense Nucleic Drug Development</i> , 1998, 8, 53-61	
	126	Crooke, S.T., "Molecular mechanisms of antisense drugs: RNase H," <i>Antisense & Nucleic Acid Drug Development</i> , 1998, XP-000946837, 8, 133-134	
	127	EPO Supplementary European Search Report dated October 16, 2002, EP 00 96 5513	
	128	Kawasake, A.M., et al., "Uniformly modified 2'-deoxy-2'-fluoro phosphorothioate oligonucleotides as nuclease-resistant antisense compounds with high affinity and specificity for RNA targets," <i>J. Med. Chem.</i> , 1993, 36, 831-841	
	129	Uhlmann, E., et al., "Antisense oligonucleotides: a new therapeutic principle," <i>Chem. Rev.</i> , 1990, 90(4), 543-584	
EXAMINER		DATE CONSIDERED	



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office				Docket No. ISIS-5138		Application No. 10/616,009	
				Applicant Stanley T. Crooke, et al.			
				Filing Date July 8, 2003		Group Not Yet Assigned	
				Confirmation No. Not Yet Assigned			
U. S. PATENT DOCUMENTS							
Examiner Initial		Document No.	Date	Name	Class	Subclass	
	130	3,687,808	08/29/72	Merigan et al.	195	28	
	131	4,981,957	01/01/91	Lebleu et al.	536	27	
	132	5,118,800	06/02/92	Smith et al.	536	23	
	133	5,212,295	05/18/93	Cook	536	26.7	
	134	5,319,080	06/07/94	Leumann	536	27.1	
	135	5,359,044	10/25/94	Cook et al.	536	23.1	
	136	5,393,878	02/28/95	Leumann	536	28.2	
	137	5,446,137	08/29/95	Maag et al.	536	23.1	
	138	5,466,786	11/14/95	Buhr et al.	536	26.26	
	139	5,514,785	05/07/96	Van Ness et al.	536	22.1	
	140	5,519,134	05/21/96	Acevedo et al.	544	243	
	141	5,567,811	10/22/96	Misiura et al.	536	25.34	
	142	5,576,208	11/19/96	Monia, et al.	435	240.2	
	143	5,576,427	11/19/96	Cook et al.	536	23.1	
	144	5,591,722	01/07/97	Montgomery et al.	514	45	
EXAMINER				DATE CONSIDERED			



Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office				Docket No. ISIS-5138		Application No. 10/616,009	
				Applicant Stanley T. Crooke, et al.			
				Filing Date July 8, 2003		Group Not Yet Assigned	
				Confirmation No. Not Yet Assigned			
U. S. PATENT DOCUMENTS							
Examiner Initial		Document No.	Date	Name	Class	Subclass	
	145	5,597,909	01/28/97	Urdea et al.	536	24.3	
	146	5,610,300	03/11/97	Altmann et al.	544	244	
	147	5,627,053	05/06/97	Usman et al.	435	91.1	
	148	5,639,649	06/17/97	Almond et al.	435	235.1	
	149	5,639,873	06/17/97	Barascut et al.	536	25.3	
	150	5,646,265	07/08/97	McGee	536	25.34	
	151	5,658,873	08/19/97	Bertsch-Frank et al.	510	375	
	152	5,670,633	09/23/97	Cook et al.	536	23.1	
	153	5,700,922	12/23/97	Cook	536	23.1	
	154	5,859,221	01/12/99	Cook et al.	536	23.1	
	155	08/398,901	03/06/95	Cook et al.			
	156	09/123,108	07/27/98	Manoharan et al.			
	157	09/344,260	06/25/99	Manoharan			
	158	09/349,040	07/07/99	Manoharan et al.			
	159	09/370,541	08/09/99	Manoharan et al.			
	160	09/378,568	08/19/99	Manoharan et al.			
EXAMINER				DATE CONSIDERED			

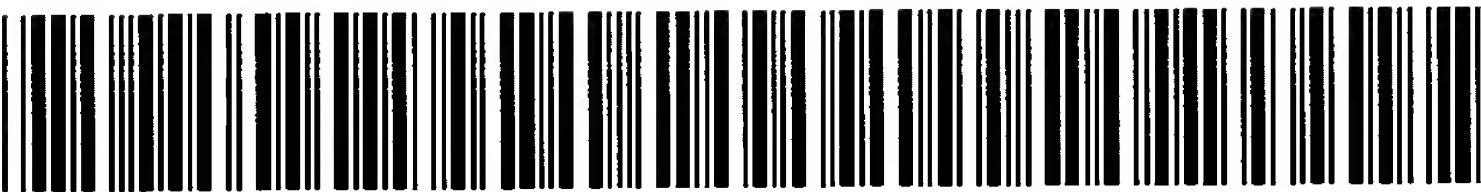


Form PTO-1449 Modified List of Patent and Publications Cited by Applicant (Use several sheets if necessary) U.S. Department of Commerce Patent and Trademark Office				Docket No. ISIS-5138		Application No. 10/616,009	
				Applicant Stanley T. Crooke, et al.			
				Filing Date July 8, 2003		Group Not Yet Assigned	
				Confirmation No. Not Yet Assigned			

U. S. PATENT DOCUMENTS						
Examiner Initial		Document No.	Date	Name	Class	Subclass
	161	5,652,355	07/29/97	Metlev, et al.	536	24.5
	162	6,001,653	12/14/99	Crooke, et al.	435	375
	163	6,121,437	09/19/00	Guzaev, et al.	536	26.1
	164	5,955,589	09/21/99	Cook, et al.	536	23.1
	165	5,672,695	09/30/97	Eckstein, et al.	536	24.5
	166	5,801,154	09/98	Baracchini, et al.	514	44
	167	5,623,065	04/97	Cook, et al.	536	23.1

FOREIGN PATENT DOCUMENTS						
Examiner Initial		Document No.	Date	Country	Translation	
					YES	NO
	168	WO 89/12060	12/14/89	PCT		
	169	0 788 366 B1	08/97	EP		

EXAMINER	DATE CONSIDERED
-----------------	------------------------



Creation date: 09-09-2003
Indexing Officer: KTO - KIM THU TO
Team: OIPE Scanning
Dossier: 10609268

Legal Date: 08-18-2003

No.	Doccode	Number of pages
1	A.PE	1
2	CLM	10
3	REM	1
4	LET.	2

Total number of pages: 14

Remarks:

Order of re-scan issued on